Respiratory Medicine CME 3 (2010) 153–155

Contents lists available at ScienceDirect

Respiratory Medicine CME

journal homepage: www.elsevier.com/locate/rmedc

Case Report

A 19–year–old man with severe obstructive lung disease

Abubakr A. Bajwa*, Faisal Usman [a], Danny Pulido [b], James D. Cury [c], Luis Laos [d]

University of Florida College of Medicine, 655 West 8th Street, Jacksonville, Fl, 32209, United States

ARTICLE INFO

Article history:
Received 21 July 2009
Accepted 4 September 2009

Keywords:
Bronchiolitis
Obstructive lung disease
Goodpasture syndrome

ABSTRACT

A 19-year-old boy presented to ambulatory clinic with shortness of breath after walking two blocks. He denied any cough, orthopnea, chest pain or hemoptysis. Ten months prior to admission he was admitted to the medical intensive care unit with respiratory failure and was diagnosed with Goodpasture syndrome. He was treated with cyclophosphamide and steroids. He was discharged home after recovering. Patient subsequently developed dyspnea on minimal exertion. Spirometry showed severe obstructive lung disease and HRCT of chest showed diffuse micronodular disease with patchy ground-glass opacities, mild bronchiectasis and bronchiolectasis. Serologies for goodpasture syndrome were normal. A diagnosis of post-Goodpasture syndrome constrictive bronchiolitis was made. Due to severity of symptoms he was treated with azithromycin. His FEV1 doubled in 3 months and in addition to significant clinical improvement the HRCT findings also improved. This is the first described case of constrictive bronciolitis developing as an aftermath of Goodpasture syndrome.

Published by Elsevier Ltd.

1. Case report

A 19-year-old man presented to ambulatory clinic with an eight month history of shortness of breath progressing to the point that he could walk only two blocks. He denied any cough, orthopnea, chest pain or hemoptysis. Approximately 10 months prior to this presentation he was admitted to the medical intensive care unit due to progressively worsening shortness of breath, non-productive cough, chills and respiratory failure. He was diagnosed with Goodpasture syndrome after a surgical lung biopsy revealed changes compatible with the diagnosis and positive anti-glomerular basement membrane antibody (Anti-GBM) serology. He was treated with cyclophosphamide and steroids. He recovered and was discharged from the hospital on oral cyclophosphamide 150 mg daily and prednisone 10 mg daily. His anti-GBM serology had stayed negative since discharge. He admitted to smoking marijuana occasionally and smoking half a pack per day of cigarettes prior to hospitalization but denied using it currently. A review of other systems was negative.

Vital signs were normal except mild resting tachycardia with pulse 103 per minute. His physical exam was normal with the exception of diminished breath sounds bilaterally with prolonged expiration.

Laboratory data was significant for an anti-GBM titer of less than 20 units (0–20), serum bicarbonate 30 meq/L (21–29), WBC count 8500/μL. Echocardiogram revealed mild global left ventricular dysfunction with ejection fraction 50–55%. Complete pulmonary function testing showed severe airflow obstruction FEV1 0.98 (26%), severely reduced DLCO (19%) and no response to bronchodilator. During a six minute walk test he walked a total of 200 m and required 3 l of oxygen to maintain his oxygen saturation at 91% at the end of the test. Postero-anterior and lateral chest radiography stable scarring from his previous lung biopsy (Fig. 1). Further evaluation with a chest CT scan showed diffuse micronodulr lung disease with evidence of bronchiectasis and bronchiolectasis (Fig. 2 A).

Patient refused to undergo bronchoscopy or to have a surgical lung biopsy done. A clinical diagnosis of post-Goodpasture's syndrome constrictive bronchiolitis was made and he was treated with azithromycin 250 mg orally three times weekly. His cyclophosphamide was stopped but prednisone was continued. He responded well to treatment. After 3 months of therapy his FEV1 improved to 1.52 (51%) and DLCO improved to 53%. His 6 min walk distance increased to 384 m and oxygen saturation improved to 90% at the end of test on room air. A repeat chest CT chest was performed (Fig. 2B).

* Corresponding author at: Division of Pulmonary, Critical Care and Sleep Medicine, University of Florida College of Medicine, 655 West 8th Street, Jacksonville, Fl, 32209, United States. Tel.: +1 904 244 4075; fax: +1 904 244 5090.
E-mail addresses: abubakr.bajwa@jax.ufl.edu (A.A. Bajwa), faisal.usman@jax.ufl.edu (F. Usman), danny.pulido@jax.ufl.edu (D. Pulido), james.cury@jax.ufl.edu (J.D. Cury), luis.laos@jax.ufl.edu (L. Laos).
[a] Tel.: +1 904 244 4075; fax: +1 904 244 5090.
[b] Tel.: +1 904 244 4075; fax: +1 904 244 5090.
[c] Tel.: +1 904 244 3071; fax: +1 904 244 5090.
[d] Tel.: +1 904 244 4075; fax: +1 904 244 5090.

1755-0017/$36.00 Published by Elsevier Ltd.
doi:10.1016/j.rmedc.2009.09.009

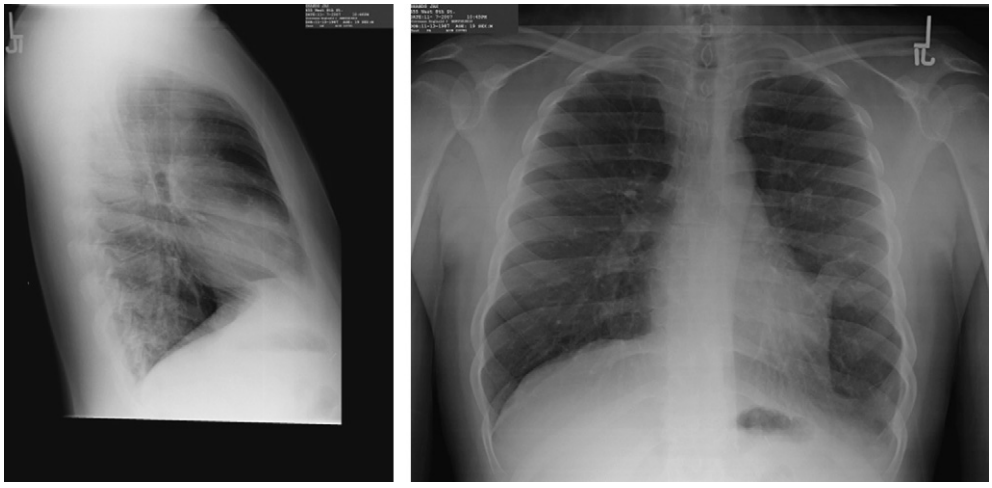

Fig. 1. Postero-anterior and lateral chest radiograph showing scarring in left lung at the site of surgical lung biopsy.

2. Discussion

Bronchiolitis is the most common disease affecting the small airways and can occur due to a variety of infectious or inflammatory causes. Although clinical, physiological, radiological and histological findings are helpful in differentiating the bronchiolar disorders, no single classification scheme for this group of disorders has been widely accepted.[1,2] The classification scheme (Table 1) proposed by Ryu et al. divides bronchiolar disorders into three major categories.[3] Based on clinical, physiological and radiological findings our patient likely had constrictive bronchiolitis. A variety of conditions (Table 2) have been associated with constrictive bronchiolitis.[3] Although constrictive bronchiolitis has been associated with a host of exposures, autoimmune, malignant and infectious etiologies, to date there have been no reports of it developing after Goodpasture syndrome.

Constrictive bronchiolitis clinically presents with sub-acute onset of cough, progressive decline in exercise tolerance and

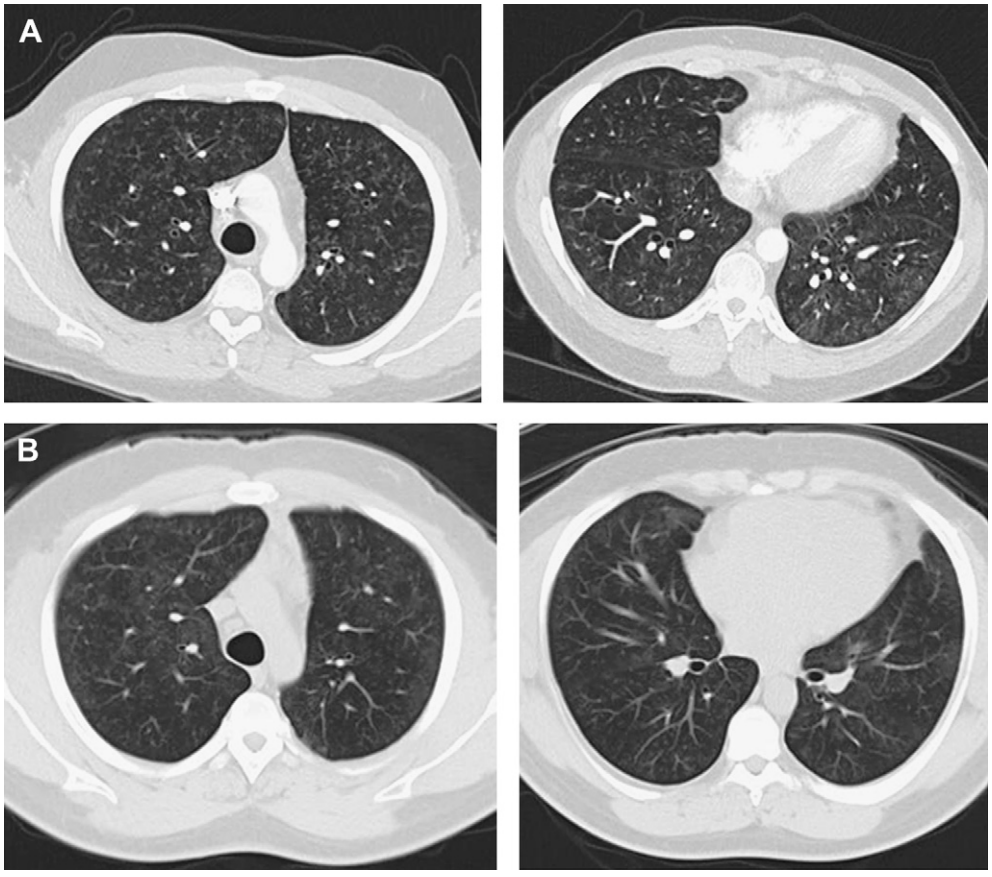

Fig. 2. A. Computed tomography of chest at baseline. B. After 3 months of therapy.

Table 1
Classification of bronchiolar disorders.

Primary bronchiolar disorders
Constrictive bronchiolitis (obliterative bronchiolitis, bronchiolitis obliterans)
Acute bronchiolitis
Diffuse panbronchioliti
Respiratory bronchiolitis (smoker's bronchiolitis)
Mineral dust airway disease
Follicular bronchiolitis
Other primary bronchiolar disorders (e.g., diffuse aspiration bronchiolitis, lymphocytic bronchiolitis)
Interstitial lung diseases with a prominent bronchiolar involvement
Hypersensitivity pneumonitis
Respiratory bronchiolitis–associated interstitial lung disease/desquamative interstitial pneumonia
Cryptogenic organizing pneumonia (idiopathic bronchiolitis obliterans organizing pneumonia or proliferative bronchiolitis)
Other interstitial lung diseases (pulmonary Langerhans' cell histiocytosis, sarcoidosis, bronchiolocentric interstitial pneumonia)
Bronchiolar involvement in large airway diseases
Chronic bronchitis
Bronchiectasis
Asthma

Table 2
Causes and underlying disorders associated with constrictive bronchiolitis.

1: Cryptogenic constrictive bronchiolitis
2: Postinfectious including most commonly viruses (adenovirus, respiratory syncytial virus, influenza, parainfluenza, etc.) and mycoplasma
3: Connective tissue diseases (rheumatoid arthritis and eosinophilic fasciitis)
4: Inhalational injury (nitrogen dioxide, sulfur dioxide, ammonia, chlorine, phosgene, hot gases, fly ash)
5: Ingested toxins (e.g., *Sauropus androgynus*)
6: Allograft recipients (heart–lung or lung transplant, bone marrow transplant)
7: Drugs (penicillamine, lomustine, cocaine, gold, penicillamine, etc.)
8: Other associations: inflammatory bowel diseases, neuroendocrine cell hyperplasia and multiple carcinoid tumorlets
9: Paraneoplastic pemphigus

worsening of dyspnea on exertion. Pulmonary function testing typically reveals evidence of airway obstruction with air trapping and reduction in diffusion capacity. High resolution CT scan (HRCT) findings include mosaic areas of decreased attenuation, peripheral bronchiectasis, bronchiolectasis, and nodular or reticulonodular opacities.[4] Given the range of etiologies that can result in constrictive bronchiolitis it is very likely that there is a host of pathogenetic mechanisms that play a role, but all leading to a similar histopathological pattern. The characteristic finding on pathology is of peribronchiolar fibrosis ranging from very subtle abnormalities to complete luminal obliteration. The inflammatory fibrosis surrounds the lumen of the bronchiole rather than filling it.[2,3] Transbronchial lung biopsy is relatively insensitive because of patchy and often subtle areas of peribronchiolar fibrosis and usually a surgical lung biopsy is needed to confirm the diagnosis. The classic features seen on HRCT in combination with pulmonary function testing and appropriate clinical setting may suffice to establish the diagnosis of constrictive bronchiolitis.

Azithromycin has been successfully used as maintenance therapy in lung transplant recipients for treatment of bronchiolitis obliterans syndrome.[5–7] Beneficial effects include not only preventing a decline in lung function but also to improving lung function in BOS. There is a progressive decline in FEV1 in patients with constrictive bronchiolitis as the result of the inflammatory response of the epithelium and its excessive repair. Azithromycin has been reported to have anti-inflammatory effects by reducing interleukin 8 and airway neutrophilia in patients with BOS.[6] HRCT may also be very helpful in following the course of constrictive bronchiolitis to document reduction in the size of nodules, bronchiolectasis and improvement of mosaic attenuation on macrolide treatment.

Our patient had the clinical features, radiological findings and pulmonary function tests that were characteristic of constrictive bronchiolitis. The fact that a significant improvement in all of these aspects occurred after 3 months of empiric therapy with low dose Azithromycin further strengthens our diagnosis.

Conflict of interest

There are neither financial disclosures nor conflict of interest for any of the authors.

References

1. Colby TV. Bronchiolitis: pathologic considerations. *Am J Clin Pathol* 1998;**109**:101–9.
2. Myrs J, Colby T. Pathological manifestations of bronchiolitis, constrictive bronchiolitis, cryptogenic organizing pneumonia, and diffuse panbronchiolitis. *Clin Chest Med* 1993;**14**:611–22.
3. Ryu JH, Myers JL, Swensen SJ. Bronchiolar disorders. *Am J Respir Crit Care Med* 2003;**168**:1277–92.
4. Lynch DA. CT of the airways, noninfectious inflammatory small airways diseases 2008:271–291.
5. Yates B, Murphy DM, Forrest IA. Azithromycin reverses airflow obstruction in established bronchiolitis obliterans syndrome. *Am J Respir Crit Care Med* 2005;**172**:772–5.
6. Verleden GM, Vanaudenaerde BM, Dupont LJ, Van Raemdonck DE. Azithromycin reduces airway neutrophilia and interleukin-8 in patients with bronchiolitis obliterans syndrome. *Am J Respir Crit Care Med* 2006;**174**:566–70.
7. Gerhardt SG, McDyer JF, Girgis RE, Conte JV, Yang SC, Orens JB. Maintenance azithromycin therapy for bronchiolitis obliterans syndrome results of a pilot study. *Am J Respir Crit Care Med* 2003;**168**:121–5.